

**REMARKS****A. March 23, 2005 Interview**

Applicants thank the Examiner for the courtesy shown in conducting an interview with the undersigned counsel on March 23, 2005. An amended claim set substantially similar to the claim set submitted herewith, was discussed. It was also noted that the pending claims of the present application are directed to a *process* for preparing a secondary standard, and methods of calibrating an instrument using a secondary standard of the present application.

More particularly, it was noted that claims 17 and 18 were amended to recite a process for preparing a secondary standard for calibrating an instrument for subsequent measurement of an analyte sample . . . *wherein the concentration of the dye is adjusted such that the fluorescent signal of the dye in the secondary standard after gelling the mixture is at least approximately equal to the fluorescent signal of a known concentration of the dye under the conditions of the analyte sample measurement.* As amended, the claims more positively recite the concept of a secondary standard. The Examiner stated that a RCE was necessary to consider the amendments. Applicants submit a RCE herewith.

**B. The Present Application**

The pending claims of the present application relate to, *inter alia*, a process for preparing a secondary standard. Secondary standards mimic a primary or ideal standard, i.e., they mimic the optical properties of the aqueous assay of interest with a known amount of dye. Unlike primary standards however, the dye is in a different and more stable medium than the medium used in a primary standard. Whereas primary standards must be prepared afresh for each calibration, secondary standards exhibit long term stability and can be used repeatedly.

The stable media used in the secondary standards of the present application include viscosity changing polymers. In various embodiments, the viscosity changing polymers are added to the container in the form of a liquid along with a dye. The viscosity changing polymer is

subsequently gelled. After gelling the viscosity changing polymer, the medium has a viscosity high enough that the standard will not pour out, or change shape upon manipulation.

Accordingly, the present application provides a process for preparing a secondary standard in which the dye and media can be easily introduced into the container, and subsequently gelled in order to provide long-term stability and convenience.

In order to account for the more-stable media used in the secondary standard, the concentration of the dye is adjusted such that the fluorescent signal of the dye is equal to a known amount of dye under the conditions of the analyte sample measurement. For example, if an instrument is being calibrated for measurements in a TRIS/HCl buffer medium, and a primary standard would otherwise be employed with 100 nM of Cy3 dye to calibrate the instrument, then the concentration of the dye in the viscosity changing polymer media is adjusted to equal the fluorescence of 100 nM of Cy3 dye in TRIS/HCL buffer (see the Example set forth on page 14-15 of the application). This step, which is now more-positively recited in the claims, provides a secondary standard that is functionally equivalent to a primary standard, with the added stability and convenience discussed above.

#### **C. Status of the Claims**

Claims 17-31 are pending and at issue. Independent claims 17, 18, and 28 have been amended as discussed above. Support for these amendments can be found, for example, on page 14, lines 9-11 of the application as-filed. No new matter has been added by this amendment.

#### **D. Rejections Under 35 U.S.C. § 102**

Claims 17-23 and 27-31 stand rejected as anticipated by Cote (U.S. Patent No. 6,485,703). Cote teaches a composition comprising an analyte sensitive compound comprised within a hydrogel. Cote states that the analyte sensitive compound may comprise a pH sensitive dye that undergoes a change in color, fluorescence or phosphorescence upon change of the medium's pH (see Cote, col. 8, lines 28-35).

Cote does not disclose a primary or secondary standard.

In response to Applicant's prior argument that Cote does not disclose or suggest a process for preparing a standard, or a process for preparing a container for calibrating an instrument, comprising gelling a mixture, the Examiner states that "[i]t is not seen that recitation 'for preparing a secondary standard' further defines the process by requiring anything other than the steps recited [in the body of the claim]." While applicants respectfully disagree, claims 17, 18 and 28 have been amended to recite in the body of the claim "wherein the concentration of the dye is adjusted such that the fluorescent signal of the dye in the secondary standard after gelling the mixture is at least approximately equal to the fluorescent signal of a known concentration of the dye under the conditions of the analyte sample measurement." Such a step is not taught or suggested in Cote, as Cote does not disclose or suggest a secondary standard, or a standard of any sort. Applicants request that the anticipation rejection be withdrawn.

**D. Rejections Under 35 U.S.C. § 103**

Claims 17-31 stand rejected as obvious over Cote in view of Little (U.S. Patent No. 6,077,669).

Little discloses use of control samples containing known starting quantities of nucleic acid sequences (Little, col. 8, lines 8-12). Little does not disclose or suggest a process involving a secondary standard, or a gelling step, as recited in claims 17-31. Instead, Little discloses employing standards with known quantities of nucleic acid sequences, which are amplified in parallel with unknown quantities of nucleic acid sequences (see Little, col. 6 line 63 to col. 7, line 4).

While the samples in Little may contain fluorescent dyes, Little does not disclose or suggest adjusting the concentration of the dye such that the fluorescent signal of the dye is at least approximately equal to the fluorescent signal of a known concentration of the dye under the conditions of the analyte sample measurement. Instead, Little conducts calibrations steps under the same conditions as the analyte sample measurement, i.e. the calibration sample and the analyte

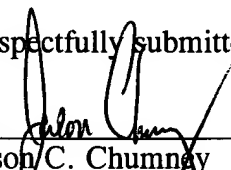
sample "are amplified in parallel during a time interval" (Little, col. 6, line 67). Accordingly, it cannot be said that Little discloses or suggests a step of adjusting the concentration of the dye in one medium such that it yields a given amount of fluorescence in a second medium -- the second medium being the conditions of the analyte sample.

Therefore Little, like Cote, does not disclose or suggest the step of "[adjusting] the concentration of the dye . . . such that the fluorescent signal of the dye in the secondary standard after gelling the mixture is at least approximately equal to the fluorescent signal of a known concentration of the dye under the conditions of the analyte sample measurement." As the cited references do not collectively teach or suggest each claim limitation, applicants request that the obviousness rejection be withdrawn.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. If the Examiner believes that an interview would be conducive to passing this application to issuance, he is respectfully requested to contact the undersigned at the number listed below.

Dated: May 31, 2005

Respectfully submitted,

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